THE FINALITY OF THE OFFICE ACTION WAS IN ERROR

Applicants request at the outset that the finality of the outstanding Office Action be withdrawn. In the first Office Action on the merits (Paper No. 7), claims 48-50, 54-57 and 59 were rejected under 35 U.S.C. § 103 in view of Valiante et al., Sambrook et al., and Aruffo et al. (*See* Paper No. 7, at p. 8.) No other obviousness rejection was asserted. In the outstanding Office Action, claims 73-89 are now rejected under 35 U.S.C. § 103 in view of Valiante et al., Sambrook et al., and Porunelloor A. Mathew et al. (See Paper No. 9, at pp. 6-7). No reason is given for the substitution of the Purunelloor A. Mathew et al. reference for the Aruffo et al. reference. Indeed, this rejection was presented as an old rejection (*see* Paper No. 9 at p. 5, second to last line, "Claims 73-89 are still rejected . . . ."). As stated by the Examiner in both actions, the "[c]laimed invention is drawn to an isolated polynucleotide encoded by the SEQ ID NO: 1 and its encoding amino acid sequence encoded by the SEQ ID NO: 2." (*See* Paper No. 7 at p. 8 and Paper No. 9 at page 6.) Thus, this new rejection was not necessitated by Applicants' amendment, and the finality of the outstanding Office Action is in error and should be withdrawn.

REJECTIONS UNDER 35 U.S.C. § 112, SECOND PARAGRAPH

Claims 73 to 84 are rejected as vague and indefinite under 35 U.S.C. § 112, second paragraph, for use of the term "comprising." The Examiner asserts that the open language of "comprising" fails to define the precise structure of the claimed nucleic acid sequences and the elements that are not taught or cannot be defined or described from the specification. (Paper No. 9 at p. 2.) Applicants believe that by this rejection is meant that the structure of the claimed isolated nucleic acid molecules is thought indefinite because transitional term "comprising" is open, and hence the isolated nucleic acid molecules may have additional sequences or elements (such as, for example, sequences encoding promoters, polyadenylation signals, replication origins, selectable markers, etc.). The Examiner requests that the claim be amended to claim "a precise sequence structure of the intended molecule(s)." By this statement, Applicants understand that if the claims were rewritten in closed language to claim an isolated nucleic acid molecule containing only the recited sequence, the rejection would not apply. This rejection is respectfully traversed.

In reviewing a claim for compliance with 35 U.S.C. § 112, second paragraph, the Examiner must consider the claim as a whole to determine whether the claim apprises one of ordinary skill in the art of its scope and, therefore, serves the notice function required by 35 U.S.C. § 112, second paragraph. *See* MPEP § 2173.02. Applicants submit that the

proper standard for definiteness under § 112 (as established in case law, and as enunciated in the Patent Office's guidelines, examining practices and procedures) has not been followed in applying this rejection.

The only reason given for rejecting the pending claims as indefinite is the use of the transitional term "comprising." There has been no assertion that the recited claim limitations are indefinite or that the public would not know whether a composition having the recited element falls within the scope of the claim. Instead, the Examiner asserts the claims are indefinite because other elements can form a structure with the recited element. But, if one of skill can tell whether the recited limitations are within the structure, the reason advanced by the Examiner is not an allowable basis for an indefiniteness rejection.

Furthermore, the term "comprising" is well established and understood, and does not in itself render claims indefinite. "Comprising," when used in claim language, means "the named elements are essential, but other elements may be added and still form a construct within the scope of the claim." *Genentech , Inc. v. Chiron Corp.*, 42 USPQ2d 1608 (Fed. Cir. 1997). "For example, a pencil structurally infringing a patent claim would not become noninfringing when incorporated into a complex machine that limits or controls what the pencil can write. Neither would infringement be negated simply because the patentee failed to contemplate use of the pencil in that environment." *A.B. Dick Co. v. Burroughs Corp.*, 218 USPQ 965 (Fed. Cir. 1983), *cert. denied*, 464 U.S. 1042 (1984).

The Examiner also asserts that additional elements are not taught or not described in the specification. Applicants submit that there is no authority under 35 U.S.C. § 112, second paragraph, which requires applicants for a patent to describe other unclaimed elements that, in combination with the recited elements, can form a structure within the scope of claims drafted in open format. Moreover, Applicants note for the record that they have described a great variety of different "elements" that can be used in combination with the recited sequences. Applicants draw the Examiner's attention to pages 33-39 of the instant specification which describes, among other things, expression plasmids, hosts, etc. In addition, Applicants have described actual working examples of isolated nucleic acid molecules containing additional "elements." For example, on page 65 of the specification, Applicants describe isolation of the clone Hup38, which comprises a NAIL cDNA cloned into the mammalian expression vector pDC409. As another example, on page 67, additional constructs made were: (1) a FLAG, poly-His tagged soluble form of NAIL encoded by DNA contained within the expression vector

pDC412; and (2) a leucine zipper, poly-His tagged soluble form of NAIL encoded by DNA contained within the expression vector pDC412.

In summary, the Examiner's request that Applicants amend their claims to recite closed language is not supported by the law under 35 U.S.C. § 112, second paragraph and, if followed, would vitiate the reasons for pursuing patent protection on Applicants' claimed invention.

Claim 79 is rejected under 35 U.S.C. § 112, second paragraph, for use of the term "fragment thereof." The Examiner states that the metes and bounds of the term are not defined (Paper No. 9 at p. 5). The Examiner asserts that the claim is interpreted in light of the specification, but the limitations of the specification are not read into the claim and therefore the claim is considered indefinite. Applicants respectfully disagree that the term as used in claim 79 is indefinite. Nevertheless, without acquiescence in the applicability of the rejection, and without prejudice to future prosecution, this claim has been cancelled.

In view of the above, Applicants request reconsideration and withdrawal of the rejections under 35 U.S.C. § 112, second paragraph.

REJECTIONS UNDER 35 U.S.C. § 112, FIRST PARAGRAPH

Claims 73-89 are rejected under 35 U.S.C. § 112, first paragraph, for lack of enablement. Although the Examiner concedes that the specification enables "an isolated nucleic acid molecule consisting of SEQ ID NO: 1 and its coding amino acid sequence SEQ ID NO: 2, wherein its functional fusion proteins are made by its amino acid residues 1-221 with tags (SEQ ID NOs: 6-8)," the Examiner asserts the specification does not reasonably provide enablement for having any or all polynucleotide or amino acids fragment thereof having 80% homology to SEQ ID NO: 1 or 2 to be a functional molecule like NAIL." (Paper No. 9 at pp. 2-3.) The rejection is traversed.

Applicants previously replied that given the disclosure of the instant application that, for one skilled in the art, (1) making homologs that are 80% identical was straightforward, and (2) testing such homologs for binding to CD48 required no undue experimentation. The Examiner acknowledges and does not rebut Applicants' previous reply that making homologs that are 80% identical is straightforward (point 1 above). However, the Examiner does not acknowledge, nor does she present any evidence to rebut, the fact that testing such homologs for binding to CD48 requires no undue experimentation (point 2 above).

Instead, the Examiner reiterates the previously cited papers by Robin et al. and Struyf et al.[1] as allegedly establishing that one amino acid mutation can change the function of the resulting molecule. Even if these references did support this allegation, these references fail to buttress the enablement rejection. In other words, these references do not establish that it would take undue experimentation to determine whether proteins which have the recited homology also have the recited biological function of binding to CD48.

The standard to be applied in assessing enablement is whether the experimentation needed to practice the claimed invention is undue or unreasonable. *See* TRAINING MATERIALS FOR EXAMINING PATENT APPLICATIONS WITH RESPECT TO 35 U.S.C. SECTION 112, FIRST PARAGRAPH-ENABLEMENT CHEMICAL/BIOTECHNICAL APPLICATIONS, *citing In re Wands*, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). Instead of applying this standard, the rejection has focused on one of the eight *Wands* factors, the alleged unpredictability in function after changing one amino acid, and relied upon this allegation for asserting the claims are only enabled for polynucleotides encoding the exact amino acid sequences used experimentally in the working examples of the application. However, unpredictability of the art is only one factor to be considered. In addition, the references relied upon to support the rejection are not evidence that the claimed invention is not enabled. They do not relate to the protein encoded by the nucleic acids of the claimed invention, they do not show in any way that making variants requires undue experimentation, and they do not show that testing variants for binding requires undue experimentation.

Applicants have requested that the Examiner provide reasons or evidence indicating why the testing of polypeptides for sequence identity, or the ability to bind CD48, would require undue experimentation. The Examiner has provided no such evidence. Accordingly, the rejection under 35 U.S.C. § 112, first paragraph, for lack of enablement is in error and should be withdrawn.

Claims 73-89 are rejected under 35 U.S.C. § 112, first paragraph, as lacking an adequate written description in the specification. The Examiner asserts that the described invention is limited to SEQ ID NOs:1, 2, 6, 7, 8, shown to have the biological properties

[1] According to the NCBI PubMed database, Struyf et al. was published in April, 1998, which is after Applicants' filing date. According to the Guidelines, generally it is inappropriate for the Examiner to use post-filing date references in an attempt to show non-enablement. *See* TRAINING MATERIALS FOR EXAMINING PATENT APPLICATIONS WITH RESPECT TO 35 U.S.C. SECTION 112, FIRST

of encoding NAIL (specifically, the ability to bind CD48), and that the specification does not provide a written description of any additional sequences. This rejection is respectfully traversed.

In maintaining the rejection, the Examiner continues to rely upon *University of California v. Eli Lilly and Co.*, 43 USPQ2d 1398 (Fed. Cir, 1997), stating that the instant "situation would be the same to the Eli Lilly Co. because some sequence generated from a host, rather than human, may accidentally have 80% homology to the SEQ ID NO: 1 or 2." Applicants submit that this statement is both unsupported by the evidence of record, and immaterial to whether the standards for written description have been met for the instantly claimed invention. Further, the Examiner does not address Applicants' point in the previous reply that the rejection is inconsistent with the USPTO's own guidelines for examination under the written description requirement.

Contrary to the Examiner's assertions and in sharp contrast to the situation is *Lilly*, the specification does indeed show that Applicants had possession of the claimed invention. Specifically, Applicants cloned the human cDNA that encodes NAIL, identified the NAIL binding partner as CD48, and described not only the nucleic acid molecules noted by the Examiner, but also contemplated and described a wide variety of variants of these molecules (*e.g.*, mutations, conserved changes, deletions, fusions to sequences encoding useful domains such as Fc's, etc.) at pages 17-33. Thus, it is clear that Applicants contemplated and were in possession of the claimed invention.

In addition, the Examiner has provided no explanation as to why her interpretation of *Lilly* is inapposite to the guidelines promulgated by the USPTO. Applicants again refer the Examiner to the USPTO's "Synopsis of Application of Written Description Guidelines" (pertinent pages enclosed with the previous response). Applicants previously referred the Examiner to Example 14, pages 53-55. The claim of Example 14 recites a protein having SEQ ID NO:3 and variants thereof that are at least 95% identical to SEQ ID NO:3 and catalyze the reaction of A->B. The disclosure of Example 14 provides a single species (SEQ ID NO:3) that has actually been reduced to practice, and describes an assay for identifying the variants having the desired catalytic activity. The analysis considers (1) whether the members of genus vary substantially from each other; and (2) whether the disclosed species is representative of the members of the genus; in order to determine whether one of skill in the art would determine if the applicant was in possession of the necessary common attributes possessed by the members of the genus.

PARAGRAPH-ENABLEMENT CHEMICAL/BIOTECHNICAL APPLICATIONS, Section V., A. Use of

For Example 14, it was determined that the member species did not substantially vary since the variants have 95% identity or greater to the reference sequence, and also possess the catalytic activity. It was also determined that the disclosed species was representative since all members must have at least 95% structural identity to SEQ ID NO:3. The analysis determined that one of skill in the art would conclude that the applicant was in possession of the necessary common attributes possessed by the members of the genus, and therefore the disclosure in this Example meets the written description requirement. Applicants submit that the polypeptides encoded by the polynucleotides of claims 73-80 can be analyzed in a similar manner to that provided in Example 14. First, the polypeptides encoded by the polynucleotides do not substantially vary as members of a genus since they all have at least 80% (or 90%) identity to SEQ IDNO:2 and possess the same binding activity. Second, the polypeptide having SEQ ID NO:2 is a representative species of the genus since all polypeptides must have at least 80% (or 90%) identity to this sequence. Therefore, one of skill in the art would conclude that the Applicants were in possession of the necessary common attributes possessed by the members of the genus, and therefore the instant specification meets the written description requirement for these claims.

In light of the statements set forth above, Applicants respectfully request that the Examiner reconsider and withdraw the rejections of the claims on the basis of the 35 U.S.C. § 112, first paragraph, written description requirement.

REJECTION UNDER 35 U.S.C. § 102

Claim 79 is rejected under 35 U.S.C. § 102(b) as anticipated by Porunelloor A. Mathew et al. (*J. Immunol.* 151, 5328-5337 (1993)). Without acquiescence in the applicability of the rejection, and without prejudice to future prosecution, this claim has been cancelled. Hence, the rejection is rendered moot and should be withdrawn.

REJECTIONS UNDER 35 U.S.C.§ 103

The Examiner states that any ground of rejection not repeated is removed. (Paper No. 9 at p. 2.) Applicants acknowledge that the rejection under 35 U.S.C. § 103 over the combination of U.S. Patent No. 5,688,690A to Valiante et al. ('690 patent), Sambrook et al. (Molecular Cloning: A Laboratory Manual, 2d Ed, pp. 2.43-2.84), and Aruffo et al.

Post-Filing Date Evidence.

(*PNAS USA* 84, 8573-8577 (1987)) has not been repeated and is therefore deemed removed.

Claims 73-89 are rejected under 35 U.S.C. § 103 over the combination of the '690 patent, Sambrook et al., and Porunelloor A. Mathew et al. (*J. Immunol.* 151 (10), 5328-5327 (1993)). This rejection is respectfully traversed.

The Examiner asserted that the claimed invention is *prima facie* obvious over this combination of references. The Examiner has stated that it would be obvious to one of ordinary skill in the art to clone the p38 molecule that is identified as existing in the '069 patent using the antibody C1.7 and the methods taught in all three references to clone the cDNA encoding it. (page 10, paper 7, second paragraph). The Porunelloor A. Mathew et al. reference is cited as disclosing a sequence having high homology to the NAIL molecule recited in the claimed invention. Applicants traverse this rejection.

To establish a prima facie case of obviousness, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings with a reasonable expectation of success. In addition, the prior art reference (or references when combined) must teach or suggest all the claim limitations. Finally, the teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in Applicant's disclosure. MPEP § 2143, *citing In re Vaeck*, 20 USPQ2d 1438 (Fed. Cir. 1991). In the instant rejection, there is no motivation to combine these three references, and the three references in combination do not teach or suggest all of the claim limitations.

With respect to motivation, the rejection impermissibly relies upon Applicants' own disclosure to combine these references. The only connection between these two references given in the Office Action is the fact that the 2B4 sequence in the Porunelloor A. Mathew et al. reference is similar to the sequence of NAIL *provided in Applicants' disclosure!* Thus, the motivation to combine these references has explicitly been gleaned from Applicants' own disclosure. Motivation to combine references must come from the prior art, not Applicants' specification. No motivation existed in the prior art to combine the Porunelloor A. Mathew et al. reference with the '690 patent. It was only when Applicants discovered and cloned the cDNA encoding human NAIL was the relationship between human NAIL and murine 2B4 realized. Using Applicants' own disclosure to combine these references is impermissible hindsight reconstruction.

In addition, the references in combination do not teach or suggest all of the claim limitations. Claims 73-88 recite particular amino acid and nucleotide ***sequences***, and these ***sequences*** are not described or suggested in any of the three references cited. Although the patent to Valiante et al. (the '069 patent) speculates as to potential methods for cloning cDNA encoding the p38 molecule, the patent does not describe or suggest any details about what the actual sequence might be. The Porunelloor A. Mathew et al. reference, even if there was some motivation in the prior art to combine with the '069 patent (which there is not), does not cure the deficiencies of the '069 patent and Sambrook et al. because it does not disclose the nucleic acid molecules claimed in claims 73-88.

Therefore, a *prima facie* case of obviousness under 35 U.S.C.§ 103 has not been made, and the rejection of the claims on this basis is improper and should be withdrawn.

CONCLUSION

In light of the foregoing remarks, Applicants submit that claims 73-89 are in condition for allowance. Applicants' attorney invites the Examiner to call her at the number below if it would be helpful in advancing the prosecution of this application.

Respectfully submitted,

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CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231, on the date indicated below.

Date: March 20, 2003

Signed: _____
Kathleen F. Prindle